In the United States Patent and Trademark Office

Serial No. _____

Appn. Filed : _____

Applicant: Vladimir Mordekhay

Appn. Title: APPARATUS AND METHOD FOR AUTOMATED SAMPLE ANALYSIS BY ATMOSPHERIC PRESSURE MATRIX ASSISTED LASER DESORPTION IONIZATION MASS SPECTROMETRY

Examiner/GAU: _____

Mailed: July 9/2003

At: San Carlos, CA

Information Disclosure Statement

Assistant Commissioner for Patents

Washington, District of Columbia 20231

Sir:

Attached is a completed Form PTO-1449 and copies of the pertinent parts of the references cited thereon. Following are comments on references pursuant to Rule 98:

U.S. Pat. 5,288,644 issued in February 22, 1994 to Ronald C. Beavis, et al. discloses an apparatus and method for the sequencing of genome. The apparatus comprises an automated DNA sampler, which adds a matrix solution

from a container to separated DNA samples. Thus, the above-described VP-MALDI technique requires that the sample plate carrier be loaded into the mass spectrometer through a vacuum lock and even though manipulations with the sample support are carried out automatically and coordinated by the computer, all sampler operations for loading the samples into the mass spectrometer are performed in vacuum. Such a system requires the use of complicated seals and special drive, transportation, and actuation mechanisms, which have to be vacuum-proof. Furthermore, the sample loading system of U.S. Pat. 5,288,644 has a relatively low throughput rate.

U.S. Reissued Patent RE 37,485 filed by Marvin L. Vestal and published on December 25, 2001 describes another a spectrometer system and method for vacuum-pressure matrix-assisted laser desorption measurements. The system is equipped with a sample plate transport mechanism for automatically inputting and outputting each of the sample plates into and from the sample-receiving chamber of the mass spectrometer. The transfer from the preparation station to the vacuum chamber and in the opposite direction is always carried out through the vacuum lock. This intermediate transfer operations delays the throughput of the system as a whole. Another disadvantage of the sample plate delivery system of the aforementioned reissued patent is that two different mechanisms are required for picking up and delivery of the sample plates to the location from where the samples are introduced into the mass spectrometer (in the above case, to the vacuum lock) and for retaining the sample plate in the aforementioned location. A serious disadvantage of the aforementioned system is that for picking up sample plates the handling mechanisms come in direct contact with each sample plate, and this increases a change of contamination of the samples and of the sample plates themselves. Another serious disadvantage of the automatic loading/unloading systems for VP-MALDI is that the mechanisms for operation in vacuum must be provided with reliable seals and

therefore such mechanisms are complicated in structure and very expensive to manufacture. They also are expensive and complicated in maintenance.

U.S. Patent No. 5,965,884 issued on October 12, 1999 to Victor V. Laiko, et al.. describes an AP-MALDI apparatus that comprises an ionization chamber, an interface for connecting the ionization chamber to a spectrometer, a sample plate or support with sample deposited on its target surface, a laser, and a lens for focusing a laser beam generated by the laser. The interface, which is usually a part of the spectrometer, comprises an inlet orifice, through which ionized analyte particles enter the spectrometer from the ionization chamber. The inlet orifice is connected to a electric power supply to serve as an electrode. However, a disadvantage of the atmospheric-pressure system of U.S. Patent No. 5,965,884 is that it is associated with manual loading/unloading procedures of the sample supports.

U.S. Patent No. 6,541,768 issued on April 1, 2003 to Bruce A. Andrien, Jr., et al. discloses a multiple sample introduction system for APCI (atmospheric pressure chemical ionization) mass spectrometry. The electrospray ion source is interfaced to a mass spectrometer, which is configured in a vacuum chamber. Individual electrospray (ES) probe assemblies can be configured in the electrospray ion source atmospheric pressure chamber, where solution is sprayed from individual probe tips. Although the system described above is intended for introduction of the samples to the vacuum chamber of the mass spectrometer from the atmospheric pressure chamber, the APCI system described above is not designed for automatically inputting and outputting each of the sample supports into and from the sample receiving chamber of the mass spectrometer. The system is rather intended for individual introduction of sample supports one-by-one in a slow sequence and therefore does not need means for automating loading or unloading of ES tips. The ampoule-like construction of the

ES-tips itself is not suitable for quick introduction of the sample into the mass spectrometer, as compared to the use of a multiple-cell sample plates.

Agilent Technologies Inc. introduced an AP-MALDI, co-developed by Masstech, Inc., by providing a sample handling interface and a laser that is capable of handling and analyzing a sample plate with multiple samples(see http://www.apmaldi.com/Products. Htm). This interface with little or no modification can be attached to various atmospheric pressure ionization mass spectrometers. The main disadvantage of the apparatus is the inconvenience of manual loading for sample plates. The autosamples, which are designed for the conventional vacuum MALDI, are too complicated and inefficient for AP-MALDI since they are designed for delivering of the sample plates into the vacuum. Also robotic systems used in stamping or welding industries with a flexible arm can be used to load the sample plates, into a commercial apparatus produced by Masstech, Inc., however these systems are complex and not designed to work directly with plates that have biological sample deposited on one side of the plate. For example, for picking up plates several commercial robotic systems use vacuum grips that can destroy or contaminate the deposited sample.

Thus, none of the references mentioned above discloses, as claimed in my main Claim 1 with dependent Claims 2-36, an apparatus for sample analysis of samples on sample plates by atmospheric pressure matrix assisted laser desorption ionization mass spectrometry in which, among other things, the grippers of transporting mechanisms handle the carriers that carry the sample plates with samples, thus protecting the sample plates and samples from contaminations that could be caused by direct contact with the grippers. Furthermore, none of the references mentioned above discloses, as claimed in my independent Claim 37, a method for sample analysis of samples on sample plates by atmospheric pressure ionization matrix assisted laser desorption

ionization mass spectrometry, wherein a combined gripper and atmospheric pressure interface unit is used as a mechanical arm of a robot for loading/unloading sample plates into and from said sample carriers storage means and at the same time for holding the sample plates during analysis.

Respectfully,

Applicant Vladimir Mordekhay

07,08,03

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PTO/SB/08A (10-01)
Approved for use through 10/31/2002. OMB 0651-0031
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Complete if Known	
Application Number	
Filing Date	
First Named Inventor	Vladimir Mordekhay
Art Unit	
Examiner Name	
Attorney Docket Number	

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Document Number: Number - Kind Code[2] (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		US- 5,288,644	1994	R. Beavis et.al	
		US- RE37,485	2001	M. Vestal	
		US- 5,965,884	1999	V. Laiko et.al.	
		US- 6,541,768	2003	B. Andrien, Jr. et.al.	
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FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Foreign Patent Document: Country Code[3] - Number[4] - Kind Code[5] (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T[6]

Examiner Signature		Date Considered	

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[1] Applicant's unique citation designation number (optional). [2] See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. [3] *Enter Office that issued the document, by the two-letter code* (WIPO Standard ST.3). [4] *For Japanese patent documents, the* indication of the year of the reign of the Emperor must precede the serial number of the patent document. [5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. [6] Applicant is to place a check mark here if English language Translation is attached.

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Complete if Known	
Application Number	
Filing Date	
First Named Inventor	Vladimir Mordekhay
Group Art Unit	
Examiner Name	
Attorney Docket Number	

OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T[2]
1.		Agilent Technologies Inc., Sample Handling Interface for AP-MALDI (see http://www.apmaldi.com/Products.htm)	

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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